

Supporting Information:

Dynamic microPET scan. NOD/SCID mouse was intravenously injected with 7.4 MBq of ^{64}Cu -DO3A-VS-Cys⁴⁰-Exendin-4 and then subjected to a 30-min dynamic scan (2×1 min, 3×3 min, 2×5 min, 1×9 min; total of 8 frames) starting right after injection. Five-minute static PET images were also acquired at 1h after injection. The images were reconstructed by 2-dimensional ordered-subsets expectation maximization (OSEM) algorithm.

Solution Stability. The solution stability of ^{64}Cu -DO3A-VS-Cys⁴⁰-Exendin-4 was studied by measuring the radiochemical purity with HPLC after incubation in serum solution at 37 °C. The purified product was reconstituted in serum solution to 1 mCi/mL. Sample of the resulting solution were analyzed by radio-HPLC at 7 h post incubation.

Metabolic Stability. The metabolic stability of ^{64}Cu -DO3A-VS-Cys⁴⁰-Exendin-4 was evaluated in a NOD/SCID mouse. Sixty minutes after the intravenous injection of 7.4 MBq of ^{64}Cu -DO3A-VS-Cys⁴⁰-Exendin-4, the mouse was sacrificed and liver and kidneys were harvested. The liver and kidneys were homogenized using a homogenizer, suspended in 1 mL of PBS buffer, and then centrifuged for 5 min at 14,000 rpm. For each sample, after the removal of the supernatant, 50% TFA in 100 μL PBS was added to the solution, followed by mixing and centrifugation for 5 min. The upper solution was then taken and injected for HPLC analysis. The eluent was collected with a fraction collector (1.0 min/fraction), and the radioactivity of each fraction was measured with a gamma counter.

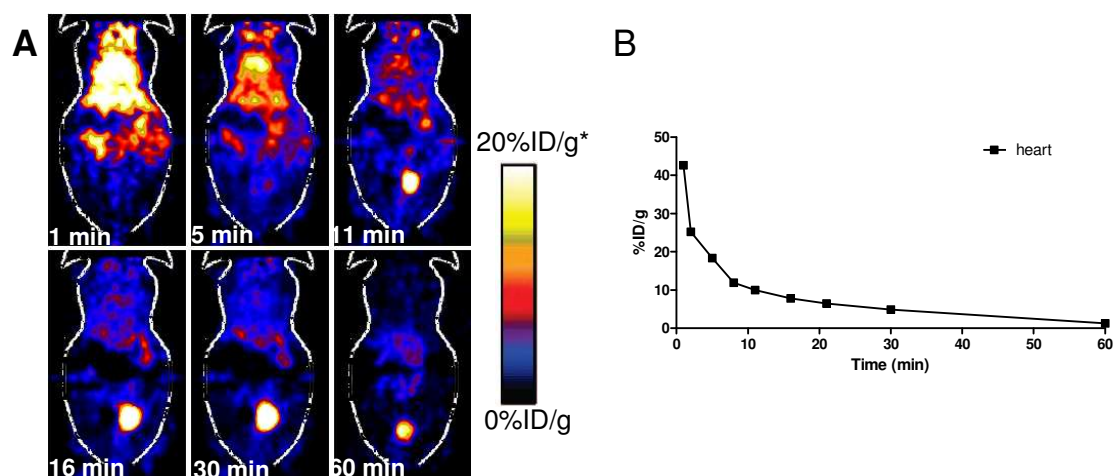


Figure S1. (A) Representative coronal microPET images of a NOD/SCID mouse at 1, 5, 11, 16, 30, and 60 min after injection of ^{64}Cu -DO3A-VS-Cys⁴⁰-Exendin-4. (B) Time-activity curves of heart after intravenous injection of ^{64}Cu -DO3A-VS-Cys⁴⁰-Exendin-4. Data were derived from a multiple time-point microPET study.

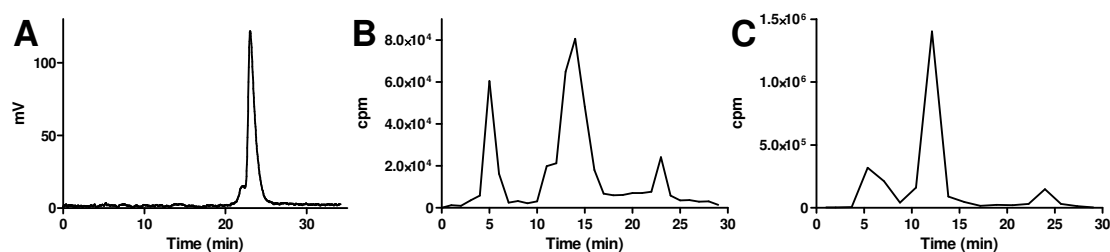


Figure S2. (A) The HPLC profile of ^{64}Cu -DO3A-VS-Cys⁴⁰-Exendin-4 at 7 h post purification. Metabolic stability of ^{64}Cu -DO3A-VS-Cys⁴⁰-Exendin-4 in the liver (B) and kidneys (C) at 1 h post-injection.